Contents of Volume 74

January 2004

i **This Month in the *Journal***
Kathryn Garber

Articles

1 **The Breakpoint Region of the Most Common Isochromosome, i(17q), in Human Neoplasia Is Characterized by a Complex Genomic Architecture with Large, Palindromic, Low-Copy Repeats**
Aikaterini Barbouti, Pawel Stankiewicz, Chad Nusbaum, Christina Cuomo, April Cook, Mattias Höglund, Bertil Johansson, Anne Hagemeijer, Sung-Sup Park, Felix Mitelman, James R. Lupski, and Thoas Fioretos

11 **The PARK8 Locus in Autosomal Dominant Parkinsonism: Confirmation of Linkage and Further Delineation of the Disease-Containing Interval**
Alexander Zimprich, Bertram Müller-Myhsok, Matthew Farrer, Petra Leitner, Manu Sharma, Mary Hulihan, Paul Lockhart, Audrey Strongosky, Jennifer Kachergus, Donald B. Calne, Jon Stoessl, Ryan J. Uitti, Ronald F. Pfeiffer, Claudia Trenkwalder, Nikolaus Homann, Erwin Ott, Karoline Wenzel, Friedrich Asmus, John Hardy, Zbigniew Wszolek, and Thomas Gasser

20 **Dissection of Genomewide-Scan Data in Extended Families Reveals a Major Locus and Oligogenic Susceptibility for Age-Related Macular Degeneration**
Sudha K. Iyengar, Danhong Song, Barbara E. K. Klein, Ronald Klein, James H. Schick, Jennifer Humphrey, Christopher Millard, Rachel Liptak, Karlie Russo, Gyungah Jun, Kristine E. Lee, Bonnie Fijal, and Robert C. Elston

40 **Population-Genetic Basis of Haplotype Blocks in the 5q31 Region**
Eric C. Anderson and Montgomery Slatkin

50 **The Effective Mutation Rate at Y Chromosome Short Tandem Repeats, with Application to Human Population-Divergence Time**
Lev A. Zhivotovsky, Peter A. Underhill, Cengiz Cinnioğlu, Manfred Kayser, Bharti Morar, Toomas Kivisild, Rosaria Scozzari, Fulvio Cruciani, Giovanni Destro-Bisol, Gabriella Spedini, Geoffrey K. Chambers, Rene J. Herrera, Kiau Kiun Yong, David Gresham, Ivailo Tournev, Marcus W. Feldman, and Luba Kalaydjieva

62 **Evidence for Extensive Transmission Distortion in the Human Genome**
Sebastian Zöllner, Xiaoquan Wen, Neil A. Hanchard, Mark A. Herbert, Carole Ober, and Jonathan K. Pritchard

73 **Linkage at 12q24 with Systemic Lupus Erythematosus (SLE) Is Established and Confirmed in Hispanic and European American Families**
Swapan K. Nath, Ana I. Quintero-Del-Rio, Jeff Kilpatrick, Lourdes Feo, Maria Ballesteros, and John B. Harley

83 **Antisense-Induced Multiexon Skipping for Duchenne Muscular Dystrophy Makes More Sense**
Annemieke Aartsma-Rus, Anneke A. M. Janson, Wendy E. Kaman, Mattie Bremmer-Bout, Gert-Jan B. van Ommen, Johan T. den Dunnen, and Judith C. T. van Deutekom

93 **Identification and Functional Analysis of *ZIC3* Mutations in Heterotaxy and Related Congenital Heart Defects**
Stephanie M. Ware, Jianlan Peng, Lirong Zhu, Susan Fernbach, Suzanne Colicos, Brett Casey, Jeffrey Towbin, and John W. Belmont

Contents of Volume 74

January 2004

i **This Month in the *Journal***
Kathryn Garber

Articles

1 **The Breakpoint Region of the Most Common Isochromosome, i(17q), in Human Neoplasia Is Characterized by a Complex Genomic Architecture with Large, Palindromic, Low-Copy Repeats**
Aikaterini Barbouti, Pawel Stankiewicz, Chad Nusbaum, Christina Cuomo, April Cook, Mattias Höglund, Bertil Johansson, Anne Hagemeijer, Sung-Sup Park, Felix Mitelman, James R. Lupski, and Thoas Fioretos

11 **The PARK8 Locus in Autosomal Dominant Parkinsonism: Confirmation of Linkage and Further Delineation of the Disease-Containing Interval**
Alexander Zimprich, Bertram Müller-Myhsok, Matthew Farrer, Petra Leitner, Manu Sharma, Mary Hulihan, Paul Lockhart, Audrey Strongosky, Jennifer Kachergus, Donald B. Calne, Jon Stoessl, Ryan J. Uitti, Ronald F. Pfeiffer, Claudia Trenkwalder, Nikolaus Homann, Erwin Ott, Karoline Wenzel, Friedrich Asmus, John Hardy, Zbigniew Wszolek, and Thomas Gasser

20 **Dissection of Genomewide-Scan Data in Extended Families Reveals a Major Locus and Oligogenic Susceptibility for Age-Related Macular Degeneration**
Sudha K. Iyengar, Danhong Song, Barbara E. K. Klein, Ronald Klein, James H. Schick, Jennifer Humphrey, Christopher Millard, Rachel Liptak, Karlie Russo, Gyungah Jun, Kristine E. Lee, Bonnie Fijal, and Robert C. Elston

40 **Population-Genetic Basis of Haplotype Blocks in the 5q31 Region**
Eric C. Anderson and Montgomery Slatkin

50 **The Effective Mutation Rate at Y Chromosome Short Tandem Repeats, with Application to Human Population-Divergence Time**
Lev A. Zhivotovsky, Peter A. Underhill, Cengiz Cinnioğlu, Manfred Kayser, Bharti Morar, Toomas Kivisild, Rosaria Scozzari, Fulvio Cruciani, Giovanni Destro-Bisol, Gabriella Spedini, Geoffrey K. Chambers, Rene J. Herrera, Kiau Kiun Yong, David Gresham, Ivailo Tournev, Marcus W. Feldman, and Luba Kalaydjieva

62 **Evidence for Extensive Transmission Distortion in the Human Genome**
Sebastian Zöllner, Xiaoquan Wen, Neil A. Hanchard, Mark A. Herbert, Carole Ober, and Jonathan K. Pritchard

73 **Linkage at 12q24 with Systemic Lupus Erythematosus (SLE) Is Established and Confirmed in Hispanic and European American Families**
Swapan K. Nath, Ana I. Quintero-Del-Rio, Jeff Kilpatrick, Lourdes Feo, Maria Ballesteros, and John B. Harley

83 **Antisense-Induced Multiexon Skipping for Duchenne Muscular Dystrophy Makes More Sense**
Annemieke Aartsma-Rus, Anneke A. M. Janson, Wendy E. Kaman, Mattie Bremmer-Bout, Gert-Jan B. van Ommen, Johan T. den Dunnen, and Judith C. T. van Deutekom

93 **Identification and Functional Analysis of *ZIC3* Mutations in Heterotaxy and Related Congenital Heart Defects**
Stephanie M. Ware, Jianlan Peng, Lirong Zhu, Susan Fernbach, Suzanne Colicos, Brett Casey, Jeffrey Towbin, and John W. Belmont

106 Selecting a Maximally Informative Set of Single-Nucleotide Polymorphisms for Association Analyses Using Linkage Disequilibrium
Christopher S. Carlson, Michael A. Eberle, Mark J. Rieder, Qian Yi, Leonid Kruglyak, and Deborah A. Nickerson

121 The Burden of Genetic Disease on Inpatient Care in a Children's Hospital
Shawn E. McCandless, Jeanne W. Brunger, and Suzanne B. Cassidy

128 Mutation of *CERKL*, a Novel Human Ceramide Kinase Gene, Causes Autosomal Recessive Retinitis Pigmentosa (RP26)
Miquel Tuson, Gemma Marfany, and Roser Gonzàlez-Duarte

139 Maternally Inherited Aminoglycoside-Induced and Nonsyndromic Deafness Is Associated with the Novel C1494T Mutation in the Mitochondrial 12S rRNA Gene in a Large Chinese Family
Hui Zhao, Ronghua Li, Qiuju Wang, Qingfeng Yan, Jian-Hong Deng, Dongyi Han, Yidong Bai, Wie-Yen Young, and Min-Xin Guan

Reports

153 Early-Onset Renal Cell Carcinoma as a Novel Extraparaganglial Component of *SDHB*-Associated Heritable Paraganglioma
Sakari Vanharanta, Mary Buchta, Sarah R. McWhinney, Sanna K. Virta, Mariola Peçzkowska, Carl D. Morrison, Rainer Lehtonen, Andrzej Januszewicz, Heikki Järvinen, Matti Juhola, Jukka-Pekka Mecklin, Eero Pukkala, Riitta Herva, Maija Kiuru, Nina N. Nupponen, Lauri A. Aaltonen, Hartmut P. H. Neumann, and Charis Eng

160 Mapping Multiple Sclerosis Susceptibility to the *HLA-DR* Locus in African Americans
Jorge R. Oksenberg, Lisa F. Barcellos, Bruce A. C. Cree, Sergio E. Baranzini, Teodorica L. Bugawan, Omar Khan, Robin R. Lincoln, Amy Swerdlin, Emmanuel Mignot, Ling Lin, Douglas Goodin, Henry A. Erlich, Silke Schmidt, Glenys Thomson, David E. Reich, Margaret A. Pericak-Vance, Jonathan L. Haines, and Stephen L. Hauser

168 A Novel Syndrome Combining Thyroid and Neurological Abnormalities Is Associated with Mutations in a Monocarboxylate Transporter Gene
Alexandra M. Dumitrescu, Xiao-Hui Liao, Thomas B. Best, Knut Brockmann, and Samuel Refetoff

176 Variation in a Repeat Sequence Determines Whether a Common Variant of the Cystic Fibrosis Transmembrane Conductance Regulator Gene Is Pathogenic or Benign
Joshua D. Groman, Timothy W. Hefferon, Teresa Casals, Lluís Bassas, Xavier Estivill, Marie Des Georges, Caroline Guittard, Monika Koudova, M. Daniele Fallin, Krisztina Nemeth, Gyorgy Fekete, Ludovit Kadasi, Ken Friedman, Martin Schwarz, Cristina Bombieri, Pier Franco Pignatti, Emmanuel Kanavakis, Maria Tzetis, Marianne Schwartz, Giuseppe Novelli, Maria Rosaria D'Apice, Agnieszka Sobczynska-Tomaszewska, Jerzy Bal, Manfred Stuhrmann, Milan Macek, Jr., Mireille Claustres, and Garry R. Cutting

180 A Large AZFc Deletion Removes *DAZ3/DAZ4* and Nearby Genes from Men in Y Haplogroup N
S. Fernandes, S. Paracchini, L. H. Meyer, G. Floridia, C. Tyler-Smith, and P. H. Vogt

Letter to the Editor

188 Novel Vitiligo Susceptibility Loci on Chromosomes 7 (*AIS2*) and 8 (*AIS3*), Confirmation of *SLEV1* on Chromosome 17, and Their Roles in an Autoimmune Diathesis
Richard A. Spritz, Katherine Gowan, Dorothy C. Bennett, and Pamela R. Fain

Book Review

192 **Hormones, Genes, and Cancer**
Edited by Brian E. Henderson, Bruce Ponder, and Ronald K. Ross
Reviewed by Mustafa Ozen

Announcements

194 **Employment Opportunities; Conference**

February 2004

i **This Month in the *Journal***
Kathryn Garber

Articles

197 **Both Rare and Common Polymorphisms Contribute Functional Variation at *CHGA*, a Regulator of Catecholamine Physiology**
Gen Wen, Sushil K. Mahata, Peter Cadman, Manjula Mahata, Sajalendu Ghosh, Nitish R. Mahapatra, Fangwen Rao, Mats Stridsberg, Douglas W. Smith, Payam Mahboubi, Nicholas J. Schork, Daniel T. O'Connor, and Bruce A. Hamilton

208 **Are Variants in the *CAPN10* Gene Related to Risk of Type 2 Diabetes? A Quantitative Assessment of Population and Family-Based Association Studies**
Yiqing Song, Tianhua Niu, JoAnn E. Manson, David J. Kwiatkowski, and Simin Liu

223 **Confirmation of Linkage to Chromosome 1q for Peak Vertebral Bone Mineral Density in Premenopausal White Women**
Michael J. Econs, Daniel L. Koller, Siu L. Hui, Tonya Fishburn, P. Michael Conneally, C. Conrad Johnston, Jr., Munro Peacock, and Tatiana M. Foroud

229 **Comparative Genomics and the Evolution of Human Mitochondrial DNA: Assessing the Effects of Selection**
J. L. Elson, D. M. Turnbull, and Neil Howell

239 **Ethylmalonic Encephalopathy Is Caused by Mutations in *ETHE1*, a Gene Encoding a Mitochondrial Matrix Protein**
Valeria Tiranti, Pio D'Adamo, Egill Briem, Gianfrancesco Ferrari, Rossana Mineri, Eleonora Lamantea, Hanna Mandel, Paolo Balestri, Maria-Teresa Garcia-Silva, Brigitte Vollmer, Piero Rinaldo, Si Houn Hahn, James Leonard, Shamima Rahman, Carlo Dionisi-Vici, Barbara Garavaglia, Paolo Gasparini, and Massimo Zeviani

253 **Genomewide Linkage Analysis for Internal Carotid Artery Intimal Medial Thickness: Evidence for Linkage to Chromosome 12**
Caroline S. Fox, L. Adrienne Cupples, Irmarie Chazaro, Joseph F. Polak, Philip A. Wolf, Ralph B. D'Agostino, Jose M. Ordovas, and Christopher J. O'Donnell

262 **Premature Myocardial Infarction Novel Susceptibility Locus on Chromosome 1P34-36 Identified by Genomewide Linkage Analysis**
Qing Wang, Shaoqi Rao, Gong-Qing Shen, Lin Li, David J. Moliterno, L. Kristin Newby, William J. Rogers, Ruth Cannata, Erich Zirzow, Robert C. Elston, and Eric J. Topol

272 Evidence of a Novel Quantitative-Trait Locus for Obesity on Chromosome 4p in Mexican Americans
Rector Arya, Ravindranath Duggirala, Christopher P. Jenkinson, Laura Almasy, John Blangero, Peter O'Connell, and Michael P. Stern

283 Pleiotropic Effects of a Chromosome 3 Locus on Speech-Sound Disorder and Reading
Catherine M. Stein, James H. Schick, H. Gerry Taylor, Lawrence D. Shriberg, Christopher Millard, Amy Kundtz-Kluge, Karlie Russo, Nori Minich, Amy Hansen, Lisa A. Freebairn, Robert C. Elston, Barbara A. Lewis, and Sudha K. Iyengar

298 Null Leukemia Inhibitory Factor Receptor (*LIFR*) Mutations in Stüve-Wiedemann/Schwartz-Jampel Type 2 Syndrome
Nathalie Dagoneau, Deborah Scheffer, Céline Huber, Lihadh I. Al-Gazali, Maja Di Rocco, Anne Godard, Jelena Martinovic, Annick Raas-Rothschild, Sabine Sigaudy, Sheila Unger, Sophie Nicole, Bertrand Fontaine, Jean-Luc Taupin, Jean-François Moreau, Andrea Superti-Furga, Martine Le Merrer, Jacky Bonaventure, Arnold Munnich, Laurence Legeai-Mallet, and Valérie Cormier-Daire

306 Inherent Bias toward the Null Hypothesis in Conventional Multipoint Nonparametric Linkage Analysis
Nicholas J. Schork and Tiffany A. Greenwood

317 Matching Strategies for Genetic Association Studies in Structured Populations
David A. Hinds, Renee P. Stokowski, Nila Patil, Karel Konvicka, David Kershenobich, David R. Cox, and Dennis G. Ballinger

326 Mutations within the *MGC4607* Gene Cause Cerebral Cavernous Malformations
C. Denier, S. Goutagny, P. Labauge, V. Krivosic, M Arnoult, A. Cousin, A. L. Benabid, J. Comoy, P. Frerebeau, B. Gilbert, J. P. Houtteville, M. Jan, F. Lapierre, H. Loiseau, P. Menei, P. Mercier, J. J. Moreau, A. Nivelon-Chevallier, F. Parker, A. M. Redondo, J. M. Scarabin, M. Tremoulet, M. Zerah, J. Maciazek, E. Tournier-Lasserve, and Société Française de Neurochirurgie

Reports

338 Pathogenic Mutations Associated with Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy Differently Affect Jagged1 Binding and Notch3 Activity via the RBP/JK Signaling Pathway
Anne Joutel, Marie Monet, Valérie Domenga, Florence Riant, and Elisabeth Tournier-Lasserve

348 Joint Analysis of the *DRD5* Marker Concludes Association with Attention-Deficit/Hyperactivity Disorder Confined to the Predominantly Inattentive and Combined Subtypes
Naomi Lowe, Aiveen Kirley, Ziarih Hawi, Pak Sham, Harvey Wickham, Christopher J. Kratochvil, Shelley D. Smith, Saretta Y. Lee, Florence Levy, Lindsey Kent, Fiona Middle, Luis A. Rohde, Tatiana Roman, Eda Tahir, Yanke Yazgan, Philip Asherson, Jonathan Mill, Anita Thapar, Antony Payton, Richard D. Todd, Timothy Stephens, Richard P. Ebstein, Iris Manor, Cathy L. Barr, Karen G. Wigg, Richard J. Sinke, Jan K. Buitelaar, Susan L. Smalley, Stan F. Nelson, Joseph Biederman, Stephen V. Faraone, and Michael Gill

357 Mutations in the *VLGR1* Gene Implicate G-Protein Signaling in the Pathogenesis of Usher Syndrome Type II
Michael D. Weston, Mirjam W. J. Luijendijk, Kurt D. Humphrey, Claes Möller, and William J. Kimberling

Letter to the Editor

367 PBAT: Tools for Family-Based Association Studies
Christoph Lange, Dawn DeMeo, Edwin K. Silverman, Scott T. Weiss, and Nan M. Laird

Announcements

370 Employment Opportunities; Conference; Call for Patients

Erratum

372 **Improving the Prediction of Complex Diseases by Testing for Multiple Disease-Susceptibility Genes**
Yang et al. (March 2003 [72:636–649])

March 2004

i **This Month in the *Journal***
Kathryn Garber

373 **2003 Cotterman Award Winners**

2003 ASHG Presidential Address

374 **Genetics, Individuality, and Medicine in the 21st Century**
David Valle

2003 William Allan Award Address

382 **Introductory Speech for Sir David Weatherall**
Yuet Wai Kan

385 **The Thalassemias: The Role of Molecular Genetics in an Evolving Global Health Problem**
David Weatherall

2003 ASHG Award for Excellence in Human Genetics Education

393 **Introductory Speech for Joan Marks**
Arno G. Motulsky

395 **The Importance of Genetic Counseling**
Joan H. Marks

2003 Curt Stern Award Address

397 **Introductory Speech for David Page**
Huntington F. Willard

399 **On Low Expectations Exceeded; or, The Genomic Salvation of the Y Chromosome**
David C. Page

Articles

403 **Genomewide Scan in Families with Schizophrenia from the Founder Population of Afrikaners Reveals Evidence for Linkage and Uniparental Disomy on Chromosome 1**
Gonçalo R. Abecasis, Rachel A. Burt, Diana Hall, Sylvia Bochum, Kimberly F. Doheny, S. Laura Lundy, Marie Torrington, J. Louw Roos, Joseph A. Gogos, and Maria Karayiorgou

418 **Assessing Whether an Allele Can Account in Part for a Linkage Signal: The Genotype-IBD Sharing Test (GIST)**
Chun Li, Laura J. Scott, and Michael Boehnke

432 Increasing the Power and Efficiency of Disease-Marker Case-Control Association Studies through Use of Allele-Sharing Information
Tasha E. Fingerlin, Michael Boehnke, and Gonçalo R. Abecasis

444 Linkage Analysis of Extremely Discordant and Concordant Sibling Pairs Identifies Quantitative Trait Loci Influencing Variation in Human Menopausal Age
Kristel M. van Asselt, Helen S. Kok, Hein Putter, Cisca Wijmenga, Petra H. M. Peeters, Yvonne T. van der Schouw, Diederick E. Grobbee, Egbert R. te Velde, Sietse Mosselman, and Peter L. Pearson

454 The African Diaspora: Mitochondrial DNA and the Atlantic Slave Trade
Antonio Salas, Martin Richards, María-Victoria Lareu, Rosaria Scozzari, Alfredo Coppa, Antonio Torroni, Vincent Macaulay, and Ángel Carracedo

466 Oculocutaneous Albinism Type 4 Is One of the Most Common Types of Albinism in Japan
Katsuhiko Inagaki, Tamio Suzuki, Hiroshi Shimizu, Norihisa Ishii, Yoshinori Umezawa, Joji Tada, Noriaki Kikuchi, Minoru Takata, Kenji Takamori, Mari Kishibe, Michi Tanaka, Yoshinori Miyamura, Shiro Ito, and Yasushi Tomita

472 Deficiency of GDP-Man:GlcNAc$_2$-PP-Dolichol Mannosyltransferase Causes Congenital Disorder of Glycosylation Type Ik
Markus Schwarz, Christian Thiel, Jürgen Lübbehusen, Bert Dorland, Tom de Koning, Kurt von Figura, Ludwig Lehle, and Christian Körner

482 Age-Related Macular Degeneration: A High-Resolution Genome Scan for Susceptibility Loci in a Population Enriched for Late-Stage Disease
Gonçalo R. Abecasis, Beverly M. Yashar, Yu Zhao, Noor M. Ghiasvand, Sepideh Zareparsi, Kari E. H. Branham, Adam C. Reddick, Edward H. Trager, Shigeo Yoshida, John Bahling, Elena Filippova, Susan Elner, Mark W. Johnson, Andrew K. Vine, Paul A. Sieving, Samuel G. Jacobson, Julia E. Richards, and Anand Swaroop

495 Incorporating Genotyping Uncertainty in Haplotype Inference for Single-Nucleotide Polymorphisms
Hosung Kang, Zhaohui S. Qin, Tianhua Niu, and Jun S. Liu

511 X-Chromosome Inactivation Patterns Are Unbalanced and Affect the Phenotypic Outcome in a Mouse Model of Rett Syndrome
Juan I. Young and Huda Y. Zoghbi

521 Human Male Recombination Maps for Individual Chromosomes
Fei Sun, Maria Oliver-Bonet, Thomas Liehr, Heike Starke, Evelyn Ko, Alfred Rademaker, Joaquima Navarro, Jordi Benet, and Renée H. Martin

532 The Levant versus the Horn of Africa: Evidence for Bidirectional Corridors of Human Migrations
J. R. Luis, D. J. Rowold, M. Regueiro, B. Caeiro, C. Cinnioğlu, C. Roseman, P. A. Underhill, L. L. Cavalli-Sforza, and R. J. Herrera

545 Congenital Disorder of Glycosylation Type Ik (CDG-Ik): A Defect of Mannosyltransferase I
Christian Kranz, Jonas Denecke, Ludwig Lehle, Kristina Sohlbach, Stefanie Jeske, Friedhelm Meinhardt, Rainer Rossi, Sonja Gudowius, and Thorsten Marquardt

Reports

552 X-Linked Mental Retardation and Autism Are Associated with a Mutation in the *NLGN4* Gene, a Member of the Neuroligin Family
Frédéric Laumonnier, Frédérique Bonnet-Brilhault, Marie Gomot, Romuald Blanc, Albert David, Marie-Pierre Moizard, Martine Raynaud, Nathalie Ronce, Eric Lemonnier, Patrick Calvas, Béatrice Laudier, Jamel Chelly, Jean-Pierre Fryns, Hans-Hilger Ropers, Ben C. J. Hamel, Christian Andres, Catherine Barthélémy, Claude Moraine, and Sylvain Briault

558 Homozygous *WNT3* Mutation Causes Tetra-Amelia in a Large Consanguineous Family
Stephan Niemann, Chengfeng Zhao, Filon Pascu, Ulrich Stahl, Ute Aulepp, Lee Niswander, James L. Weber, and Ulrich Müller

564 Intracranial Aneurysms in Finnish Families: Confirmation of Linkage and Refinement of the Interval to Chromosome 19q13.3
Monique van der Voet, Jane M. Olson, Helena Kuivaniemi, Doreen M. Dudek, Magdalena Skunca, Antti Ronkainen, Mika Niemelä, Juha Jääskeläinen, Juha Hernesniemi, Katariina Helin, Eira Leinonen, Moumita Biswas, and Gerard Tromp

572 Melanocortin-4 Receptor Gene Variant I103 Is Negatively Associated with Obesity
Frank Geller, Kathrin Reichwald, Astrid Dempfle, Thomas Illig, Caren Vollmert, Stephan Herpertz, Winfried Siffert, Matthias Platzer, Claudia Hess, Thomas Gudermann, Heike Biebermann, H.-Erich Wichmann, Helmut Schäfer, Anke Hinney, and Johannes Hebebrand

Letters to the Editor

582 Multiple Comparisons in Studies of Gene × Gene and Gene × Environment Interaction
Peter Kraft

584 Reply to Kraft
Ana Maria Valdes, Brian Rhees, and Henry Erlich

585 Revisiting the Clinical Validity of Multiplex Genetic Testing in Complex Diseases
A. Cecile J. W. Janssens, M. Carolina Pardo, Ewout W. Steyerberg, and Cornelia M. van Duijn

588 Revisiting the Clinical Validity of Multiplex Genetic Testing in Complex Diseases: Reply to Janssens et al.
Quanhe Yang, Muin J. Khoury, Lorenzo Botto, J. M. Friedman, and W. Dana Flanders

589 Impact of Genotyping Errors on Type I Error Rate of the Haplotype-Sharing Transmission/Disequilibrium Test (HS-TDT)
Michael Knapp and Tim Becker

591 Reply to Knapp and Becker
Shuanglin Zhang, Qiuying Sha, Huann-sheng Chen, Jianping Dong, and Renfang Jiang

Announcements

594 Employment Opportunities; Conference

Errata

598 Characterization of FMR1 Promoter Elements by In Vivo-Footprinting Analysis
Schwemmle et al. (June 1997 [60:1354–1362])

598 Mutations of von Hippel-Lindau Tumor-Suppressor Gene and Congenital Polycythemia
Pastore et al. (August 2003 [73:412–419])

598 A Novel Syndrome Combining Thyroid and Neurological Abnormalities Is Associated with Mutations in a Monocarboxylate Transporter Gene
Dumitrescu et al. (January 2004 [74:168–175])

April 2004

i **This Month in the *Journal***
Kathryn Garber

Review Article

599 **Epigenetics and Assisted Reproductive Technology: A Call for Investigation**
Emily L. Niemitz and Andrew P. Feinberg

Articles

610 **Haplotype Diversity across 100 Candidate Genes for Inflammation, Lipid Metabolism, and Blood Pressure Regulation in Two Populations**
Dana C. Crawford, Christopher S. Carlson, Mark J. Rieder, Dana P. Carrington, Qian Yi, Joshua D. Smith, Michael A. Eberle, Leonid Kruglyak, and Deborah A. Nickerson

623 **Crohn Disease: Frequency and Nature of CARD15 Mutations in Ashkenazi and Sephardi/Oriental Jewish Families**
Turgut Tukel, Adel Shalata, Daniel Present, Daniel Rachmilewitz, Lloyd Mayer, Deniera Grant, Neil Risch, and Robert J. Desnick

637 **Natural Selection and Molecular Evolution in *PTC*, a Bitter-Taste Receptor Gene**
Stephen Wooding, Un-kyung Kim, Michael J. Bamshad, Jennifer Larsen, Lynn B. Jorde, and Dennis Drayna

647 **Novel Analytical Methods Applied to Type 1 Diabetes Genome-Scan Data**
Flemming Pociot, Allan E. Karlsen, Claus B. Pedersen, Mogens Aalund, Jørn Nerup, and the European Consortium for IDDM Genome Studies

661 **The Western and Eastern Roots of the Saami—the Story of Genetic "Outliers" Told by Mitochondrial DNA and Y Chromosomes**
Kristiina Tambets, Siiri Rootsi, Toomas Kivisild, Hela Help, Piia Serk, Eva-Liis Loogväli, Helle-Viivi Tolk, Maere Reidla, Ene Metspalu, Liana Pliss, Oleg Balanovsky, Andrey Pshenichnov, Elena Balanovska, Marina Gubina, Sergey Zhadanov, Ludmila Osipova, Larisa Damba, Mikhail Voevoda, Ildus Kutuev, Marina Bermisheva, Elza Khusnutdinova, Vladislava Gusar, Elena Grechanina, Jüri Parik, Erwan Pennarun, Christelle Richard, Andre Chaventre, Jean-Paul Moisan, Lovorka Barać, Marijana Peričić, Pavao Rudan, Rifat Terzić, Ilia Mikerezi, Astrida Krumina, Viesturs Baumanis, Slawomir Koziel, Olga Rickards, Gian Franco De Stefano, Nicholas Anagnou, Kalliopi I. Pappa, Emmanuel Michalodimitrakis, Vladimir Ferák, Sandor Füredi, Radovan Komel, Lars Beckman, and Richard Villems

683 **Power for Genetic Association Studies with Random Allele Frequencies and Genotype Distributions**
Walter T. Ambrosius, Ethan M. Lange, and Carl D. Langefeld

694 **The Etruscans: A Population-Genetic Study**
Cristiano Vernesi, David Caramelli, Isabelle Dupanloup, Giorgio Bertorelle, Martina Lari, Enrico Cappellini, Jacopo Moggi-Cecchi, Brunetto Chiarelli, Loredana Castrì, Antonella Casoli, Francesco Mallegni, Carles Lalueza-Fox, and Guido Barbujani

705 **Variations in *GABRA2*, Encoding the α2 Subunit of the $GABA_A$ Receptor, Are Associated with Alcohol Dependence and with Brain Oscillations**
Howard J. Edenberg, Danielle M. Dick, Xiaoling Xuei, Huijun Tian, Laura Almasy, Lance O. Bauer, Raymond R. Crowe, Alison Goate, Victor Hesselbrock, Kevin Jones, Jennifer Kwon, Ting-Kai Li, John I. Nurnberger, Jr., Sean J. O'Connor, Theodore Reich, John Rice, Marc A. Schuckit, Bernice Porjesz, Tatiana Foroud, and Henri Begleiter

Reports

715 Paradoxical NSD1 Mutations in Beckwith-Wiedemann Syndrome and 11p15 Anomalies in Sotos Syndrome
Geneviève Baujat, Marlène Rio, Sylvie Rossignol, Damien Sanlaville, Stanislas Lyonnet, Martine Le Merrer, Arnold Munnich, Christine Gicquel, Valérie Cormier-Daire, and Laurence Colleaux

721 Mutations in *LRP5* or *FZD4* Underlie the Common Familial Exudative Vitreoretinopathy Locus on Chromosome 11q
Carmel Toomes, Helen M. Bottomley, Richard M. Jackson, Katherine V. Towns, Sheila Scott, David A. Mackey, Jamie E. Craig, Li Jiang, Zhenglin Yang, Richard Trembath, Geoffrey Woodruff, Cheryl Y. Gregory-Evans, Kevin Gregory-Evans, Michael J. Parker, Graeme C. M. Black, Louise M. Downey, Kang Zhang, and Chris F. Inglehearn

731 A Dual Phenotype of Periventricular Nodular Heterotopia and Frontometaphyseal Dysplasia in One Patient Caused by a Single *FLNA* Mutation Leading to Two Functionally Different Aberrant Transcripts
Martin Zenker, Anita Rauch, Andreas Winterpacht, Andreas Tagariello, Cornelia Kraus, Thomas Rupprecht, Heinrich Sticht, and André Reis

738 Identification of 51 Novel Exons of the *Usher Syndrome Type 2A (USH2A)* Gene That Encode Multiple Conserved Functional Domains and That Are Mutated in Patients with Usher Syndrome Type II
Erwin van Wijk, Ronald J. E. Pennings, Heleen te Brinke, Annemarie Claassen, Helger G. Yntema, Lies H. Hoefsloot, Frans P. M. Cremers, Cor. W. R. J. Cremers, and Hannie Kremer

745 Ribose-5-Phosphate Isomerase Deficiency: New Inborn Error in the Pentose Phosphate Pathway Associated with a Slowly Progressive Leukoencephalopathy
Jojanneke H. J. Huck, Nanda M. Verhoeven, Eduard A. Struys, Gajja S. Salomons, Cornelis Jakobs, and Marjo S. van der Knaap

752 High Proportion of Mutant Osteoblasts Is Compatible with Normal Skeletal Function in Mosaic Carriers of Osteogenesis Imperfecta
Wayne A. Cabral and Joan C. Marini

761 Germline Mutations of the Paired–Like Homeobox 2B (*PHOX2B*) Gene in Neuroblastoma
Delphine Trochet, Franck Bourdeaut, Isabelle Janoueix-Lerosey, Anne Deville, Loïc de Pontual, Gudrun Schleiermacher, Carole Coze, Nicole Philip, Thierry Frébourg, Arnold Munnich, Stanislas Lyonnet, Olivier Delattre, and Jeanne Amiel

765 A Simple Correction for Multiple Testing for Single-Nucleotide Polymorphisms in Linkage Disequilibrium with Each Other
Dale R. Nyholt

770 Nonmuscle Myosin Heavy-Chain Gene *MYH14* Is Expressed in Cochlea and Mutated in Patients Affected by Autosomal Dominant Hearing Impairment (DFNA4)
Francesca Donaudy, Rik Snoeckx, Markus Pfister, Hans-Peter Zenner, Nikolaus Blin, Mariateresa Di Stazio, Antonella Ferrara, Carmen Lanzara, Romina Ficarella, Frank Declau, Carsten M. Pusch, Peter Nürnberg, Salvatore Melchionda, Leopoldo Zelante, Ester Ballana, Xavier Estivill, Guy Van Camp, Paolo Gasparini, and Anna Savoia

Letter to the Editor

777 Novel Truncating Mutations in the *Polyglutamine Tract Binding Protein 1* Gene (*PQBP1*) Cause Renpenning Syndrome and X-Linked Mental Retardation in Another Family with Microcephaly
Claus Lenski, Fatima Abidi, Alfons Meindl, Alice Gibson, Matthias Platzer, R. Frank Kooy, Herbert A. Lubs, Roger E. Stevenson, Juliane Ramser, and Charles E. Schwartz

Book Reviews

781 **Huntington's Disease**
Edited by Gillian Bates, Peter Harper, and Lesley Jones
Reviewed by P. Hemachandra Reddy

782 **Entwined Lives: Twins and What They Tell Us About Human Behavior**
Written by Nancy Segal
Reviewed by F. Clarke Fraser

Announcements

783 **Employment Opportunities; Conference; Awards; Call for Abstracts; Cell Lines and Panels Available; Lecture**

Errata

788 **The Burden of Genetic Disease on Inpatient Care in a Children's Hospital**
McCandless et al. (January 2004 [74:121–127])

788 **The Levant versus the Horn of Africa: Evidence for Bidirectional Corridors of Human Migrations**
Luis et al. (March 2004 [74:532–544])

May 2004

i **This Month in the *Journal***
Kathryn Garber

Obituary

789 **Ching Chun Li (1912–2003): A Personal Remembrance of a Hero of Genetics**
Aravinda Chakravarti

Review Articles

793 **Myotonic Dystrophy: RNA Pathogenesis Comes into Focus**
Laura P. W. Ranum and John W. Day

805 **The Fragile-X Premutation: A Maturing Perspective**
Paul J. Hagerman and Randi J. Hagerman

Articles

817 **Bietti Crystalline Corneoretinal Dystrophy Is Caused by Mutations in the Novel Gene *CYP4V2***
Anren Li, Xiaodong Jiao, Francis L. Munier, Daniel F. Schorderet, Wenliang Yao, Fumino Iwata, Mutsuko Hayakawa, Atsushi Kanai, Muh Shy Chen, Richard Alan Lewis, John Heckenlively, Richard G. Weleber, Elias I. Traboulsi, Qingjiong Zhang, Xueshan Xiao, Muriel Kaiser-Kupfer, Yuri V. Sergeev, and J. Fielding Hejtmancik

827 Where West Meets East: The Complex mtDNA Landscape of the Southwest and Central Asian Corridor
Lluís Quintana-Murci, Raphaëlle Chaix, R. Spencer Wells, Doron M. Behar, Hamid Sayar, Rosaria Scozzari, Chiara Rengo, Nadia Al-Zahery, Ornella Semino, A. Silvana Santachiara-Benerecetti, Alfredo Coppa, Qasim Ayub, Aisha Mohyuddin, Chris Tyler-Smith, S. Qasim Mehdi, Antonio Torroni, and Ken McElreavey

846 Positional Cloning by Linkage Disequilibrium
Nikolas Maniatis, Andrew Collins, Jane Gibson, Weihua Zhang, William Tapper, and Newton E. Morton

856 Analyses of Genetic Structure of Tibeto-Burman Populations Reveals Sex-Biased Admixture in Southern Tibeto-Burmans
Bo Wen, Xuanhua Xie, Song Gao, Hui Li, Hong Shi, Xiufeng Song, Tingzhi Qian, Chunjie Xiao, Jianzhong Jin, Bing Su, Daru Lu, Ranajit Chakraborty, and Li Jin

866 Polymorphisms in the Low-Density Lipoprotein Receptor–Related Protein 5 *(LRP5)* Gene Are Associated with Variation in Vertebral Bone Mass, Vertebral Bone Size, and Stature in Whites
Serge L. Ferrari, Samuel Deutsch, Urmila Choudhury, Thierry Chevalley, Jean-Philippe Bonjour, Emmanouil T. Dermitzakis, René Rizzoli, and Stylianos E. Antonarakis

876 Genomewide Linkage Scan Identifies a Novel Susceptibility Locus for Restless Legs Syndrome on Chromosome 9p
Shenghan Chen, William G. Ondo, Shaoqi Rao, Lin Li, Qiuyun Chen, and Qing Wang

886 Genomewide Linkage Analysis of Bipolar Disorder by Use of a High-Density Single-Nucleotide–Polymorphism (SNP) Genotyping Assay: A Comparison with Microsatellite Marker Assays and Finding of Significant Linkage to Chromosome 6q22
F. A. Middleton, M. T. Pato, K. L. Gentile, C. P. Morley, X. Zhao, A. F. Eisener, A. Brown, T. L. Petryshen, A. N. Kirby, H. Medeiros, C. Carvalho, A. Macedo, A. Dourado, I. Coelho, J. Valente, M. J. Soares, C. P. Ferreira, M. Lei, M. H. Azevedo, J. L. Kennedy, M. J. Daly, P. Sklar, and C. N. Pato

898 Natural Selection and Population History in the Human Angiotensinogen Gene (*AGT*): 736 Complete *AGT* Sequences in Chromosomes from Around the World
Toshiaki Nakajima, Stephen Wooding, Takuro Sakagami, Mitsuru Emi, Katsushi Tokunaga, Gen Tamiya, Tomoaki Ishigami, Satoshi Umemura, Batmunkh Munkhbat, Feng Jin, Jia Guan-jun, Ikuo Hayasaka, Takafumi Ishida, Naruya Saitou, Karel Pavelka, Jean-Marc Lalouel, Lynn B. Jorde, and Ituro Inoue

917 Rare Autosomal Recessive Cardiac Valvular Form of Ehlers-Danlos Syndrome Results from Mutations in the *COL1A2* Gene That Activate the Nonsense-Mediated RNA Decay Pathway
Ulrike Schwarze, Ryu-Ichiro Hata, Victor A. McKusick, Hiroshi Shinkai, H. Eugene Hoyme, Reed E. Pyeritz, and Peter H. Byers

931 The Genetic Architecture of Selection at the Human Dopamine Receptor D4 (*DRD4*) Gene Locus
E. Wang, Y.-C. Ding, P. Flodman, J. R. Kidd, K. K. Kidd, D. L. Grady, O. A. Ryder, M. A. Spence, J. M. Swanson, and R. K. Moyzis

945 Little Loss of Information Due to Unknown Phase for Fine-Scale Linkage-Disequilibrium Mapping with Single-Nucleotide–Polymorphism Genotype Data
A. P. Morris, J. C. Whittaker, and D. J. Balding

954 Novel *PMS2* Pseudogenes Can Conceal Recessive Mutations Causing a Distinctive Childhood Cancer Syndrome
Michel De Vos, Bruce E. Hayward, Susan Picton, Eamonn Sheridan, and David T. Bonthron

965 Design and Analysis of Admixture Mapping Studies
C. J. Hoggart, M. D. Shriver, R. A. Kittles, D. G. Clayton, and P. M. McKeigue

979 Methods for High-Density Admixture Mapping of Disease Genes
Nick Patterson, Neil Hattangadi, Barton Lane, Kirk E. Lohmueller, David A. Hafler, Jorge R. Oksenberg, Stephen L. Hauser, Michael W. Smith, Stephen J. O'Brien, David Altshuler, Mark J. Daly, and David Reich

1001 A High-Density Admixture Map for Disease Gene Discovery in African Americans
Michael W. Smith, Nick Patterson, James A. Lautenberger, Ann L. Truelove, Gavin J. McDonald, Alicja Waliszewska, Bailey D. Kessing, Michael J. Malasky, Charles Scafe, Ernest Le, Philip L. De Jager, Andre A. Mignault, Zeng Yi, Guy de Thé, Myron Essex, Jean-Louis Sankalé, Jason H. Moore, Kwabena Poku, John P. Phair, James J. Goedert, David Vlahov, Scott M. Williams, Sarah A. Tishkoff, Cheryl A. Winkler, Francisco M. De La Vega, Trevor Woodage, John J. Sninsky, David A. Hafler, David Altshuler, Dennis A. Gilbert, Stephen J. O'Brien, and David Reich

Reports

1014 Phylogeographic Analysis of Haplogroup E3b (E-M215) Y Chromosomes Reveals Multiple Migratory Events Within and Out Of Africa
Fulvio Cruciani, Roberta La Fratta, Piero Santolamazza, Daniele Sellitto, Roberto Pascone, Pedro Moral, Elizabeth Watson, Valentina Guida, Eliane Beraud Colomb, Boriana Zaharova, João Lavinha, Giuseppe Vona, Rashid Aman, Francesco Calì, Nejat Akar, Martin Richards, Antonio Torroni, Andrea Novelletto, and Rosaria Scozzari

1023 Origin, Diffusion, and Differentiation of Y-Chromosome Haplogroups E and J: Inferences on the Neolithization of Europe and Later Migratory Events in the Mediterranean Area
Ornella Semino, Chiara Magri, Giorgia Benuzzi, Alice A. Lin, Nadia Al-Zahery, Vincenza Battaglia, Liliana Maccioni, Costas Triantaphyllidis, Peidong Shen, Peter J. Oefner, Lev A. Zhivotovsky, Roy King, Antonio Torroni, L. Luca Cavalli-Sforza, Peter A. Underhill, and A. Silvana Santachiara-Benerecetti

1035 *MSH2* c.1452–1455delAATG Is a Founder Mutation and an Important Cause of Hereditary Nonpolyposis Colorectal Cancer in the Southern Chinese Population
Tsun Leung Chan, Yee Wai Chan, Judy W. C. Ho, Celine Chan, Annie S. Y. Chan, Emily Chan, Polly W. Y. Lam, Chun Wah Tse, Kam Cheong Lee, Chi Wai Lau, Elaine Gwi, Suet Yi Leung, and Siu Tsan Yuen

1043 Mutations in *AXIN2* Cause Familial Tooth Agenesis and Predispose to Colorectal Cancer
Laura Lammi, Sirpa Arte, Mirja Somer, Heikki Järvinen, Päivi Lahermo, Irma Thesleff, Sinikka Pirinen, and Pekka Nieminen

1051 Fragile-X–Associated Tremor/Ataxia Syndrome (FXTAS) in Females with the *FMR1* Premutation
R. J. Hagerman, B. R. Leavitt, F. Farzin, S. Jacquemont, C. M. Greco, J. A. Brunberg, F. Tassone, D. Hessl, S. W. Harris, L. Zhang, T. Jardini, L. W. Gane, J. Ferranti, L. Ruiz, M. A. Leehey, J. Grigsby, and P. J. Hagerman

1057 Linkage Disequilibrium Mapping of Schizophrenia Susceptibility to the *CAPON* Region of Chromosome 1q22
Linda M. Brzustowicz, Jaime Simone, Paria Mohseni, Jared E. Hayter, Kathleen A. Hodgkinson, Eva W. C. Chow, and Anne S. Bassett

1064 Identification of a Novel Gene (*HSN2*) Causing Hereditary Sensory and Autonomic Neuropathy Type II through the Study of Canadian Genetic Isolates
Ronald G. Lafrenière, Marcia L. E. MacDonald, Marie-Pierre Dubé, Julie MacFarlane, Mary O'Driscoll, Bernard Brais, Sébastien Meilleur, Ryan R. Brinkman, Owen Dadivas, Terry Pape, Christèle Platon, Chris Radomski, Jenni Risler, Jay Thompson, Ana-Maria Guerra-Escobio, Gudarz Davar, Xandra O. Breakefield, Simon N. Pimstone, Roger Green, William Pryse-Phillips, Y. Paul Goldberg, H. Banfield Younghusband, Michael R. Hayden, Robin Sherrington, Guy A. Rouleau, and Mark E. Samuels

Book Review

1074 Inferring Phylogenies
Written by Joseph Felsenstein
Reviewed by Stephen Wooding

Announcements

1075 Employment Opportunities; Conference; Course; ABGC Diplomates

Erratum

1080 Incorrect Received Dates
Brant et al. (December 2003 [73:1282–1292]), Fox et al. (February 2004 [74:253–261]), Wang et al. (February 2004 [74:262–271]), Arya et al. (February 2004 [74:272–282]), and Weston et al. (February 2004 [74:357–366])

June 2004

i This Month in the *Journal*
Kathryn Garber

Perspective

1081 Relevance of Connexin Deafness (DFNB1) to Human Evolution
Walter E. Nance and Michael J. Kearsey

Articles

1088 Graphical Modeling of the Joint Distribution of Alleles at Associated Loci
Alun Thomas and Nicola J. Camp

1102 The T Allele of a Single-Nucleotide Polymorphism 13.9 kb Upstream of the Lactase Gene (*LCT*) (*C − 13.9kbT*) Does Not Predict or Cause the Lactase-Persistence Phenotype in Africans
Charlotte A. Mulcare, Michael E. Weale, Abigail L. Jones, Bruce Connell, David Zeitlyn, Ayele Tarekegn, Dallas M. Swallow, Neil Bradman, and Mark G. Thomas

1111 Genetic Signatures of Strong Recent Positive Selection at the Lactase Gene
Todd Bersaglieri, Pardis C. Sabeti, Nick Patterson, Trisha Vanderploeg, Steve F. Schaffner, Jared A. Drake, Matthew Rhodes, David E. Reich, and Joel N. Hirschhorn

1121 Fibroblast Growth Factor 20 Polymorphisms and Haplotypes Strongly Influence Risk of Parkinson Disease
Joelle M. van der Walt, Maher A. Noureddine, Raja Kittappa, Michael A. Hauser, William K. Scott, Ron McKay, Fengyu Zhang, Jeffrey M. Stajich, Kenichiro Fujiwara, Burton L. Scott, Margaret A. Pericak-Vance, Jeffery M. Vance, and Eden R. Martin

1128 DNA/RNA Helicase Gene Mutations in a Form of Juvenile Amyotrophic Lateral Sclerosis (ALS4)
Ying-Zhang Chen, Craig L. Bennett, Huy M. Huynh, Ian P. Blair, Imke Puls, Joy Irobi, Ines Dierick, Annette Abel, Marina L. Kennerson, Bruce A. Rabin, Garth A. Nicholson, Michaela Auer-Grumbach, Klaus Wagner, Peter De Jonghe, John W. Griffin, Kenneth H. Fischbeck, Vincent Timmerman, David R. Cornblath, and Phillip F. Chance

1136 Linkage Analysis of a Complex Disease through Use of Admixed Populations
Xiaofeng Zhu, Richard S. Cooper, and Robert C. Elston

1154 Genomewide Significant Linkage to Recurrent, Early-Onset Major Depressive Disorder on Chromosome 15q
Peter Holmans, George S. Zubenko, Raymond R. Crowe, J. Raymond DePaulo Jr., William A. Scheftner, Myrna M. Weissman, Wendy N. Zubenko, Sandra Boutelle, Kathleen Murphy-Eberenz, Dean MacKinnon, Melvin G. McInnis, Diana H. Marta, Philip Adams, James A. Knowles, Madeleine Gladis, Jo Thomas, Jennifer Chellis, Erin Miller, and Douglas F. Levinson

1168 Comparative Genomic Hybridization–Array Analysis Enhances the Detection of Aneuploidies and Submicroscopic Imbalances in Spontaneous Miscarriages
Anthony J. Schaeffer, June Chung, Konstantina Heretis, Andrew Wong, David H. Ledbetter, and Christa Lese Martin

1175 CHEK2*1100delC and Susceptibility to Breast Cancer: A Collaborative Analysis Involving 10,860 Breast Cancer Cases and 9,065 Controls from 10 Studies
The CHEK2 Breast Cancer Case-Control Consortium

1183 A Comprehensive Survey of Human Y-Chromosomal Microsatellites
Manfred Kayser, Ralf Kittler, Axel Erler, Minttu Hedman, Andrew C. Lee, Aisha Mohyuddin, S. Qasim Mehdi, Zoë Rosser, Mark Stoneking, Mark A. Jobling, Antti Sajantila, and Chris Tyler-Smith

1198 Extended Linkage Disequilibrium Surrounding the Hemoglobin E Variant Due to Malarial Selection
Jun Ohashi, Izumi Naka, Jintana Patarapotikul, Hathairad Hananantachai, Gary Brittenham, Sornchai Looareesuwan, Andrew G. Clark, and Katsushi Tokunaga

1209 Mutations of the Ephrin-B1 Gene Cause Craniofrontonasal Syndrome
Ilse Wieland, Sibylle Jakubiczka, Petra Muschke, Monika Cohen, Hannelore Thiele, Klaus L. Gerlach, Ralf H. Adams, and Peter Wieacker

1216 Somatic and Germline Instability of the ATTCT Repeat in Spinocerebellar Ataxia Type 10
Tohru Matsuura, Ping Fang, Xi Lin, Mehrdad Khajavi, Kuniko Tsuji, Astrid Rasmussen, Raji P. Grewal, Madhureeta Achari, Maria E. Alonso, Stefan M. Pulst, Huda Y. Zoghbi, David L. Nelson, Benjamin B. Roa, and Tetsuo Ashizawa

1225 Highly Significant Linkage to the *SLI1* Locus in an Expanded Sample of Individuals Affected by Specific Language Impairment
The SLI Consortium (SLIC)

Reports

1239 Mutations in the Human *TBX4* Gene Cause Small Patella Syndrome
Ernie M. H. F. Bongers, Pascal H. G. Duijf, Sylvia E. M. van Beersum, Jeroen Schoots, Albert van Kampen, Andreas Burckhardt, Ben C. J. Hamel, František Lošan, Lies H. Hoefsloot, Helger G. Yntema, Nine V. A. M. Knoers, and Hans van Bokhoven

1249 Mutated *MESP2* Causes Spondylocostal Dysostosis in Humans
Neil V. Whittock, Duncan B. Sparrow, Merridee A. Wouters, David Sillence, Sian Ellard, Sally L. Dunwoodie, and Peter D. Turnpenny

1255 The Novel Gene Encoding a Putative Transmembrane Protein Is Mutated in Gnathodiaphyseal Dysplasia (GDD)
Satoshi Tsutsumi, Nobuyuki Kamata, Tamara J. Vokes, Yutaka Maruoka, Koichi Nakakuki, Shoji Enomoto, Ken Omura, Teruo Amagasa, Masaru Nagayama, Fumiko Saito-Ohara, Johji Inazawa, Maki Moritani, Takashi Yamaoka, Hiroshi Inoue, and Mitsuo Itakura

1262 Penetrance and Expressivity of *MSH6* Germline Mutations in Seven Kindreds Not Ascertained by Family History
Barbara M. Buttin, Matthew A. Powell, David G. Mutch, Sheri A. Babb, Phyllis C. Huettner, Tina Bocker Edmonston, Thomas J. Herzog, Janet S. Rader, Randall K. Gibb, Alison J. Whelan, and Paul J. Goodfellow

1270 Offspring Gender Ratio and the Rate of Recurrent Spontaneous Miscarriages in Jewish Women at High Risk for Breast/Ovarian Cancer
Inbar Gal, Siegal Sadetzki, Ruth Gershoni-Baruch, Bernice Oberman, Howard Carp, Moshe Z. Papa, Tal Diestelman-Menachem, Shlomit Eisenberg-Barzilai, and Eitan Friedman

1276 AICA-Ribosiduria: A Novel, Neurologically Devastating Inborn Error of Purine Biosynthesis Caused by Mutation of *ATIC*
Sandrine Marie, Bénédicte Heron, Pierre Bitoun, Thérèse Timmerman, Georges Van den Berghe, and Marie-Françoise Vincent

1282 Chromosomal Abnormalities among Offspring of Childhood-Cancer Survivors in Denmark: A Population-Based Study
Jeanette Falck Winther, John D. Boice Jr., John J. Mulvihill, Marilyn Stovall, Kirsten Frederiksen, E. Janet Tawn, and Jørgen H. Olsen

1286 Disruption of *Contactin 4* (*CNTN4*) Results in Developmental Delay and Other Features of 3p Deletion Syndrome
Thomas Fernandez, Thomas Morgan, Nicole Davis, Ami Klin, Ashley Morris, Anita Farhi, Richard P. Lifton, and Matthew W. State

1294 Bias toward the Null Hypothesis in Model-Free Linkage Analysis Is Highly Dependent on the Test Statistic Used
Heather J. Cordell

1303 Missense Mutation in Pseudouridine Synthase 1 (*PUS1*) Causes Mitochondrial Myopathy and Sideroblastic Anemia (MLASA)
Yelena Bykhovskaya, Kari Casas, Emebet Mengesha, Aida Inbal, and Nathan Fischel-Ghodsian

1309 Insulin Receptor Splicing Alteration in Myotonic Dystrophy Type 2
R. S. Savkur, A. V. Philips, T. A. Cooper, J. C. Dalton, M. L. Moseley, L. P. W. Ranum, and J. W. Day

1314 A Genomewide Scan Identifies Novel Early-Onset Primary Open-Angle Glaucoma Loci on 9q22 and 20p12
J. L. Wiggs, S. Lynch, G. Ynagi, M. Maselli, J. Auguste, E. A. Del Bono, L. M. Olson, and J. L. Haines

Letters to the Editor

1321 Modes of Action of HLA-DR Susceptibility Specificities in Multiple Sclerosis
Helena Modin, Wiveka Olsson, Jan Hillert, and Thomas Masterman

1322 Nuclear Factor TDP-43 Binds to the Polymorphic TG Repeats in CFTR Intron 8 and Causes Skipping of Exon 9: A Functional Link with Disease Penetrance
Emanuele Buratti, Antonia Brindisi, Franco Pagani, and Francisco E. Baralle

Book Review

1326 Lost Paradises and the Ethics of Research and Publication
Edited by Francisco M. Salzano and A. Magdalena Hurtado
Reviewed by Trudy R. Turner

Announcements

1328 Conferences

1332 Contents of Volume 74

Information for Contributors